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Exhibit C

4

Anatomy of the Visual Sensory System

JOEL S. GLASER

The retina, optic nerves, chiasm, tracts, lateral geniculate nuclei, geniculocalcarine radiations, calcarine cortices, visual associational areas, and related interhemispheral connections comprise the primary visual-sensory system in man. This specialized afferent system crosses at right angles to the major ascending sensory and descending motor systems of the cerebral hemispheres (Fig 4-1), and in its anterior portion, it is intimately related to the vascular and bony structures at the base of the brain. As such, the visual pathways have great localizing value in neurologic diagnosis. The dominant role of vision in man may be expressed mathematically by comparing the number of nerve fibers in an optic nerve (approximately 1.2 million) with neurons in the cochlear division of an acoustic nerve (approximately 31,000) (1); therefore, the ratio of afferent neurons in the peripheral visual apparatus to the number in the aural system is roughly 40:1.

FUNCTIONAL ORGANIZATION

RETINA

Functional organization of the visual sensory system begins at the retinal level. The complex vertical and horizontal organization of retinal elements, synaptic patterns, receptor field physiology, and details of visual signal propagation are beyond the scope of this present work. The reader is referred to the excellent paper of Dowling (2), and the lucid review of control of retinal sensitivity by Werblin (3).

The distribution of visual function across the retina is not uniform but takes a pattern of concentric zones increasing in sensitivity toward the center, the fovea. Ultimately, retinal sensitivity is dictated by the cytoarchitecture of the percipient elements, which at the fovea consist of a "rod-free" central bouquet of 100,000 slender cones. The entire posterior aspect of the retina is dominated by the foveal and parafoveal cone system which occupies an area approximately 1.5 mm in diameter. The ganglion cells subserving the central cone system send axons directly to the temporal aspect of the optic disc, forming the papillomacular bundle. This "direct access route" is not encroached on by other axons originating in the temporal retina, which must curve above and below the papillomacular bundle, forming dense arcuate bands (Fig 4-2).

Østerberg (4) studied the arrangement of rods and cones in the human retina and found a skewed distribution with rod and cone densities greater in the superonasal retina than in the inferotemporal portion. Van Buren (5) performed ganglion cell counts which demonstrated the same eccentric pattern, especially in the one-cell layer which reached nearly twice as far on the nasal side of the fovea as on the temporal. This asymmetric distribution of retinal elements is reflected in the asymmetry of nasal vs temporal field and accounts for the relative foreshortening of the nasal field (6).

Although it has previously been considered that nerve fibers arising from peripheral retinal ganglion cells occupy a more superficial position in the nerve fiber layer, Ogden (7) has demonstrated that nerve fibers intermingle freely along the intraretinal course of the arcuate bundles. Segregation of fibers to bring those from the far retinal periphery to the periphery of the nerve and those from nearer the disc to an axial location must occur at the disc edge or more posteriorly.

OPTIC DISC

The optic disc is the exit site of all retinal ganglion-cell axons, collectively termed the nerve fiber layer. The disc (alternatively, nerve head or papilla) is located 3 to 4 mm nasal to the fovea and represents a 1.5 × 2.0 mm hiatus in the sclera, choroid, retinal pigment epithelium, and retina proper. There are no percipient elements on the disc, which

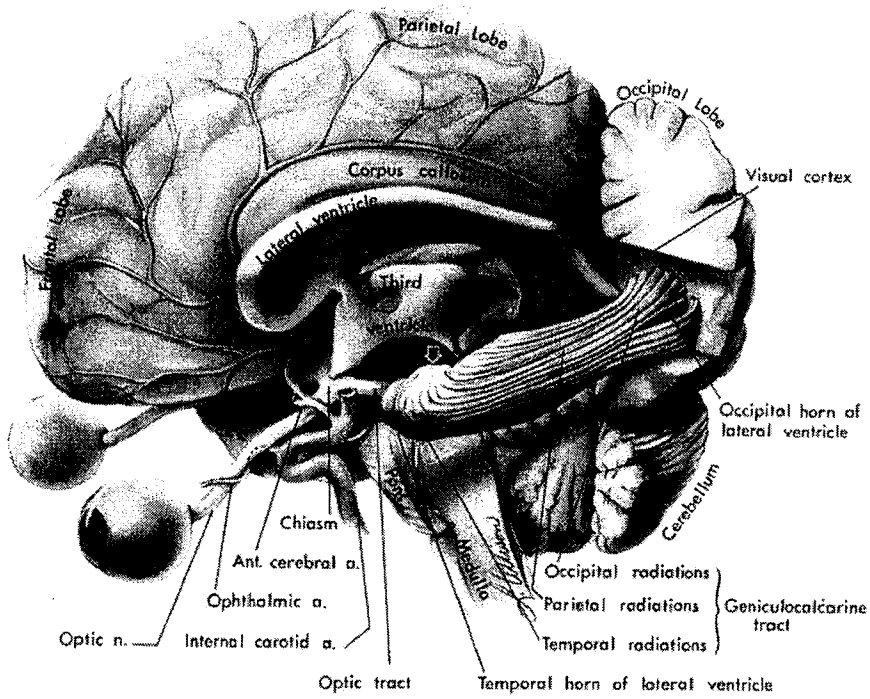


Fig 4-1. The visual-sensory system. The left cerebral hemisphere has been removed with exception of occipital lobe and ventricular system. The left lateral geniculate body is hidden (*arrow*). Note the following relationships: optic nerve with internal carotid and anterior communicating arteries; chiasm in the floor of the third ventricle; forward sweep of temporal radiations around lateral ventricle; course of occipital radiations toward interhemispheral surface of occipital lobe. The cerebral falx and cerebellar tentorium are not illustrated.

is projected in visual space as an absolute scotoma, the blind spot of Mariotte.

OPTIC NERVE

The structure of the optic nerve head in primates has been admirably brought up to date by Anderson (8–12). As the nerve fibers turn sharply to leave the plane of the retina, they are collected into fascicles and supported by glial columns composed primarily of astrocytes (Fig 4-3). The axons then exit the globe by passing through a sievelike portion of sclera, the lamina cribrosa. Just posterior to the lamina, the nerve fibers become myelinated and the diameter of the nerve enlarges to 3 to 4 mm. In the retrolaminar portion of the optic nerve, oligodendrocytes constitute two thirds of the interstitial cells and are responsible for the formation of myelin sheaths around visual axons. In peripheral nerves the Schwann cells serve this function. Therefore, the optic nerve is really a white-matter tract of the brain rather than a peripheral nerve. The orbital and intracanalicular portions of the optic nerve contain a well-developed septal system derived from pia mater, which extends at right angles into the substance of the nerve dividing it into parallel columns of variable size. Astrocytes are intimately related to the pial septa and play a role in the support and nutrition of axons.

At a point approximately 1 cm posterior to the globe, a major branch of the ophthalmic artery pierces the inferior aspect of the dural sheath of the optic nerve, gains an axial position, and emerges on the surface of the disc as the central retinal artery. For the most part, the central retinal artery does not contribute to the blood supply of the laminar and prelaminar portion of the nerve head. This area is supplied by an incomplete anastomotic arterial circle (Zinn-Haller), with contributions from the posterior ciliary arteries, pial arterial network, and peripapillary choroid (Fig 4-4). Therefore, the blood supply of the nerve head itself is primarily

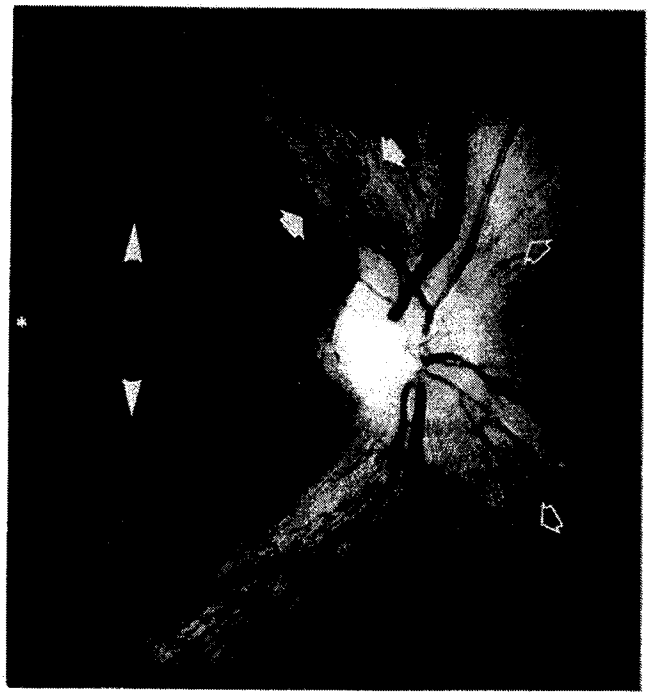


Fig 4-2. Retinal nerve fiber layer pattern. The dense temporal arcuate fiber bundles (*solid arrows*) are most easily seen. Nasal fibers (*open arrows*) take a more direct radial course. The papillomacular bundle (*arrow heads*) is most difficult to visualize.

derived from choroidal and posterior ciliary vessels, while the retina is supplied by the central retinal artery (12, 13).

The intraorbital segment of optic nerve is 25 to 30 mm long, although the distance from the back of the globe to the orbital apex is only 20 mm. Therefore, in the orbit the optic nerve has a somewhat redundant and sinuous course which may be related to free movement of the globe. At the orbital apex the nerve enters the bony optic canal, surrounded by the origins of the superior, medial, and inferior recti muscles (the so-called annulus of Zinn). The optic canal forms an angle of approximately 35° with the midsaggital plane as it runs posteromedially and is 4 to 10 mm in length (Fig 4-5). Along with the optic nerve, the canal transmits the ophthalmic artery, branches of the carotid sympathetic plexus and prolongations of the intracranial meninges which form the sheaths of the nerve. In the optic canal, the dura of the nerve and periosteum of the bone are fused, but the subarachnoid space communicates with the intracranial subarachnoid and contains cerebrospinal fluid. The rare occurrence of free passage of intracranial subarachnoid air into the orbital portions of the optic nerves has been reported (14). The optic nerves leave their canals and converge at the chiasm in the floor of the third ventricle. The nerves ascend toward the chiasm at an angle of approximately 45° with the nasotuberculum line (Fig 4-6) and average 17.1± 2.5 mm in length, such that the chiasm itself sits 10.7± 2.4 mm above the dorsum of the sella turcica (15). The relationship of the optic nerves and chiasm to the sellar area is exceedingly important and is discussed subsequently.

CHIASM

The optic chiasm is contiguous with the anteroinferior floor of the third ventricle, and it measures approximately 8 mm from anterior to posterior notch, 12 mm across and 4 mm in height. As the internal carotid arteries curve posteriorly and upward out of the cavernous sinuses, they lie immediately below the optic nerves. The carotids then ascend vertically alongside the lateral aspects of the chiasm (Fig 4-1). The precommunicating portions of the anterior cerebral arteries are closely related to the superior surface of the chiasm and optic nerves. Bergland et al (16, 17) have studied the anatomic variations in the position of the chiasm as well as its arterial supply, but it is difficult to draw conclusions regarding preferential vulnerability of one portion or another of the chiasm on the basis of blood supply. As a rule, when field defects are present due to mass lesions, there is major struc-

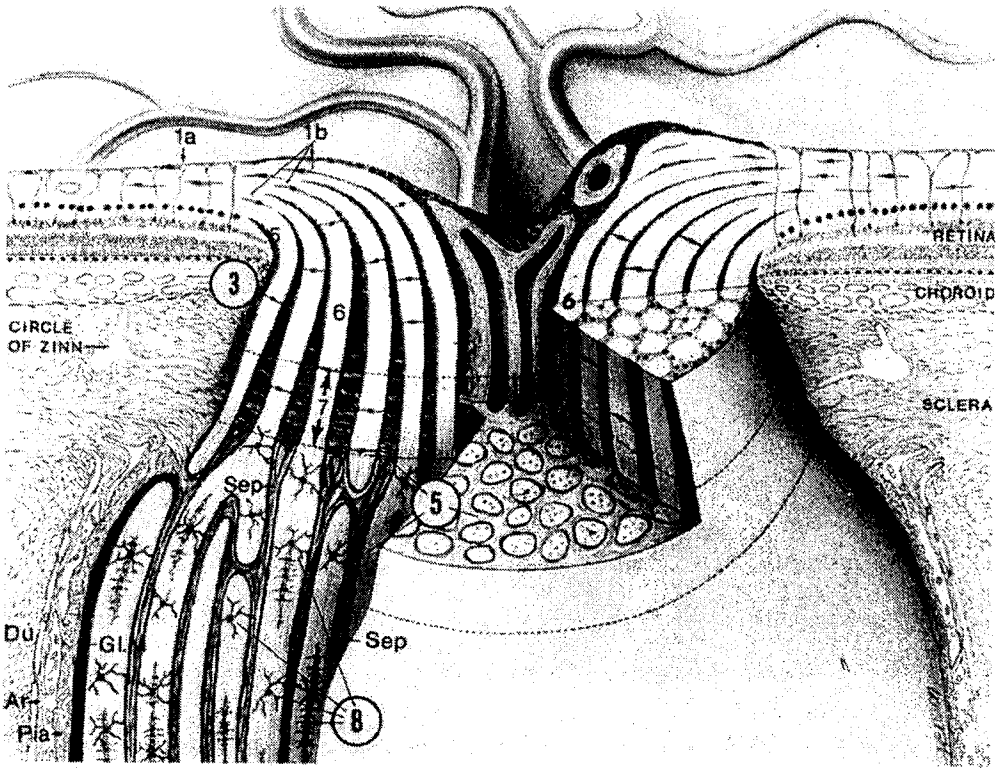


Fig 4-3. Schematic structure of optic disc and nerve. 1a, internal limiting membrane of retina; 1b, nerve fiber layer; 2, optic cup, lined by astroglial cells, and central retinal vessels; 3, ophthalmoscopically visible disc edge; 5, glial and connective tissue columns; 6, nerve fiber fascicles; 7, major portion of lamina cribrosa; 8, oligodendrocytes; Du, dura; Ar, arachnoid; Pia, pia; Gl. M, glial mantle; Sep, pial septum. (Modified from Anderson DR, Hoyt WF: Ultrastructure of intraorbital portion of human and monkey optic nerve. Arch Ophthalmol 82:506, 1969.)

tural distortion, with elevation and stretching of the chiasm and nerves. The role of mechanical compression alone cannot be evaluated. The retinotopic projection of nerve fibers through the chiasm is discussed elsewhere.

OPTIC TRACTS AND LATERAL GENICULATE NUCLEUS

The optic tracts commence from the posterior aspect of the chiasm, diverge, and sweep posteriorly around the cerebral peduncles to terminate in the lateral geniculate nuclei. These nuclei of the visual thalamus are located at the posterior extremities of the choroidal fissures, between the hippocampal gyri on the mesial aspects of the temporal lobes and the cerebral peduncles. Pupillomotor fibers leave the optic tracts anterior to the lateral geniculate bodies and gain the pretectal area via the brachium of the superior colliculus.

The lateral geniculate body is the terminus for the afferent fibers of the anterior visual pathways. Here, crossed and uncrossed fibers are organized into alternating layers (Fig 4-7), and the final visual neurons originate, forming the geniculocalcarine radiations.

VISUAL RADIATIONS

The optic radiations (geniculocalcarine tract) fan laterally and inferiorly from the lateral geniculate body, sweeping around the anterior aspect of the temporal horn of the lateral ventricles, and pass posteriorly in a relatively narrow fillet, the external sagittal striatum (Fig 4-1). The most anteroinferior fibers form a bend (Meyer's loop) which

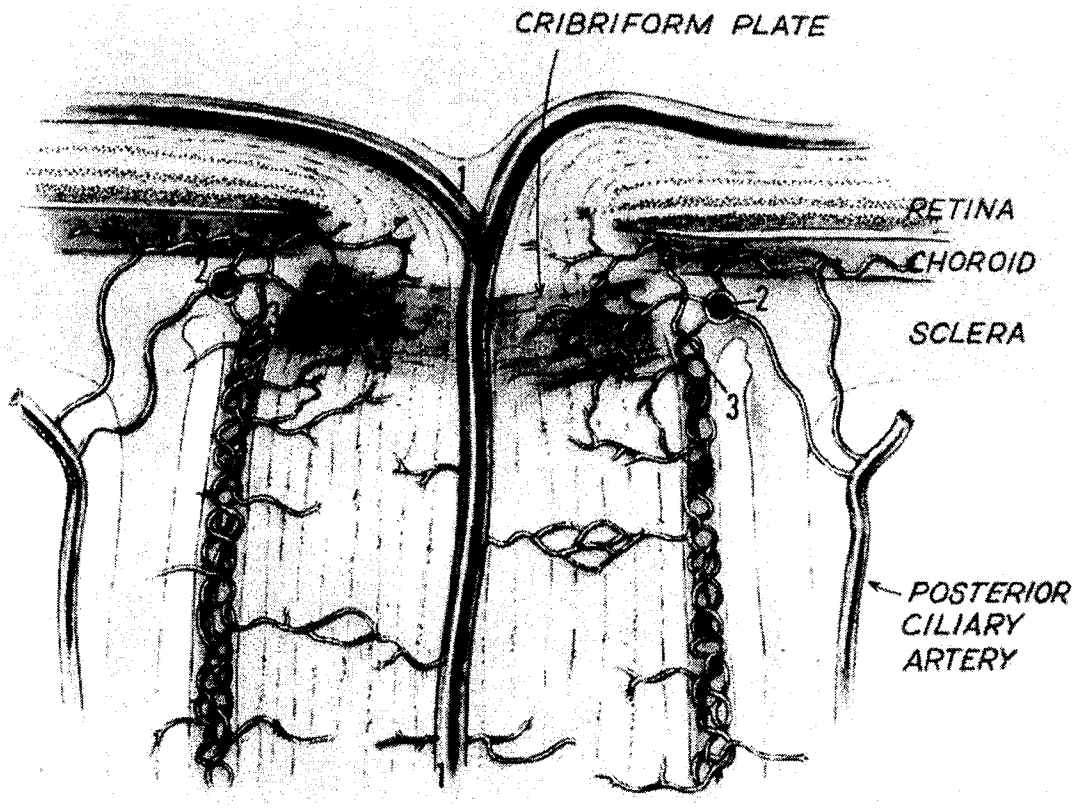


Fig 4-4. Blood supply of the optic nerve head. 1, central retinal artery; 2, arterial circle of Zinn-Haller; 3, pial arterial network. Contribution to Zinn-Haller circle from posterior ciliary arteries, pial plexus, and peripapillary choroid; the latter also sends branches directly to prelaminar disc substance. (Modified from Kolker AE, Hetherington J, Jr.: Becker-Shaffer's Diagnosis and Therapy of the Glaucomas, ed 3. St. Louis: Mosby, 1970.)

contains the projection of inferior retinal fibers and passes near or around the tip of the temporal ventricular horn. This configuration in the anterior portion of the radiations provides an explanation for the superior quadrantafiopic field defect pattern encountered in some temporal lobe lesions.

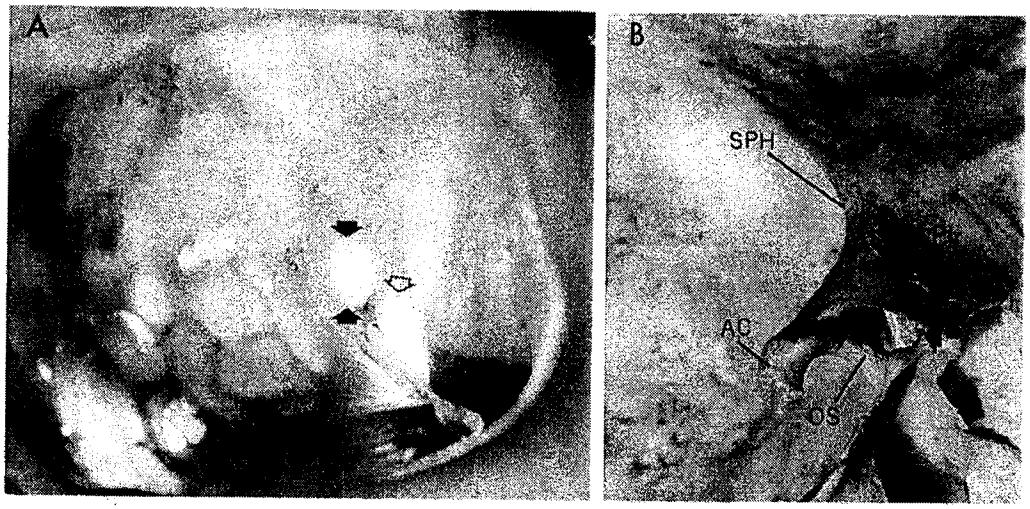
Deep in the parietal lobe, the optic radiations lie just external to the trigone and occipital horn of the lateral ventricle. Fibers pass above and below the latter to terminate in the mesial surface of the occipital lobe, the striate (calcarine) cortex.

OCCIPITAL CORTEX

The primary visual cortex (area 17) lies in the interhemispheral fissure in relationship to the falx cerebri (Fig 4-8). However, the macular projection area may extend 1 to 2 cm laterally onto the posterior surface of the occipital pole. The visual cortex extends anteriorly toward the splenium of the corpus callosum and is separated into a superior and inferior portion by the calcarine fissure. (See below and Figure 4-11.)

VISUAL ASSOCIATION AREAS AND INTERHEMISPHERAL CONNECTIONS

In order for the visual environment to be analyzed, recognized and interpreted, afferent information must be processed by higher visual associational areas. Area 18 (parastriate cortex) serves to integrate the two halves of the visual fields via a major interhemispheric commisural pathway that traverses the splenium of the corpus callosum. Thus, areas 17, 18, and 19 in one hemisphere are interconnected to areas 17, 18, and 19 in the other. It is



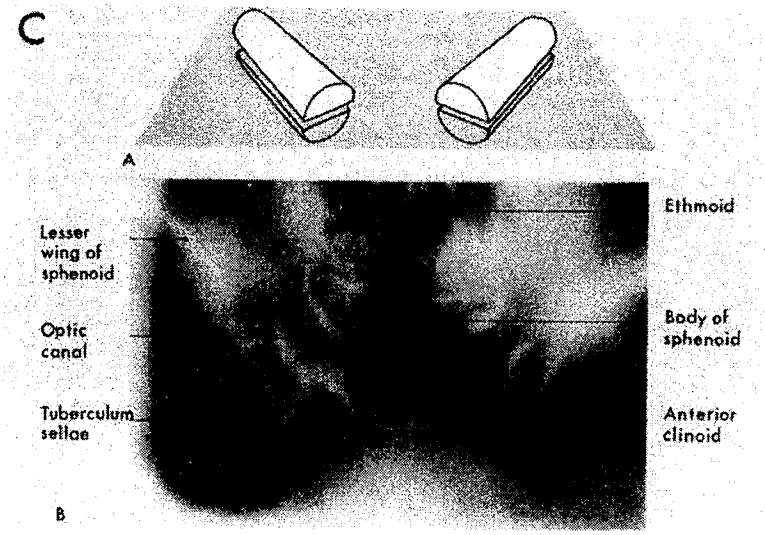


Fig 4-5. The optic canal. **A.** Anterior view of left orbital apex. Orbital end of optic canal is vertically oval (*black arrows*) and separated from superior orbital fissure (*open arrow*) by optic strut. Note transilluminated ethmoidal and sphenoidal air cells which form medial orbital wall and medial wall of optic canal. **B.** Posterior view of intracranial aspect of left optic canal demonstrating horizontally oval contour. The optic strut (OS) forms the ventrolateral margin of the canal and separates it from the carotid artery. In this preparation the ethmoidal and sphenoidal air cells have been opened. AC, anterior clinoid; PL, planum; SPH, sphenoidal wing. **C.** Tomographic section of optic canals in upper diagram. Normal axial tomogram below. (Illustration **C** from Harwood-Nash DC: Optic gliomas and pediatric neuroradiology. Radiol Clin North Am 10:83, 1972.)

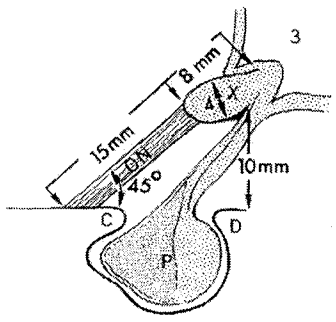


Fig 4-6. Relationships of the optic nerves (ON) and chiasm (X) to the sellar structures and third ventricle (3). C, anterior clinoid; D, dorsum sellae; P, pituitary gland in sella.

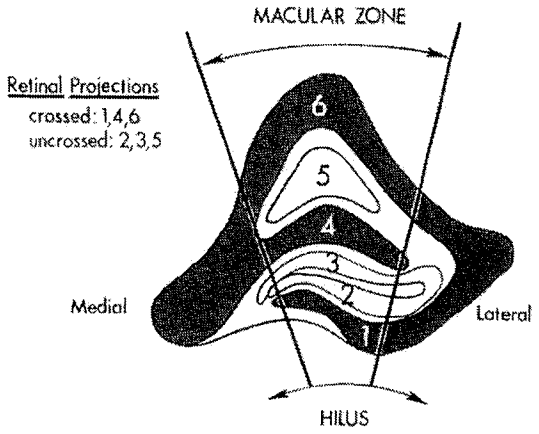


Fig 4-7. Coronal section of lateral geniculate nucleus. Note extensive macular representation.

likely that area 18 participates in sensory-motor eye coordination via fronto-occipital pathways and perhaps is the site of origin of corticomesencephalic optomotor pathways concerned with smooth pursuit of visual targets.

Area 19 (peristriate cortex) accounts for the major lateral expanse of the occipital lobe and extends into the posterior parietal and temporal lobes. Area 19 is the major parietal center for the integration of visual information.

RETINOTOPIC ORGANIZATION

Visual space is represented on the retina in a direct point-to-point relationship. Because of the optical system of the eye, the superior visual field is projected onto inferior retina and the nasal field onto temporal retina. In general, this inverted relationship holds true throughout the visual system, including optic nerves and chiasm, radiations, and cortex.

The "retinotopic" projection of visual fibers through the anterior visual pathways has been carefully mapped by Hoyt et al (18-20) utilizing retinal photocoagulation and axonal-degeneration staining techniques. Much of the following discussion is derived from that work.

The vast majority of visual fibers in the nerves and chiasm are derived from the large population of retinal "midget" ganglion cells (Polyak) subserving macular vision. Potts et al (21) have analyzed the axonal population in the primate optic nerve with special reference to foveal outflow. Those authors found the total number of optic nerve fibers in man to be 1.1 to 1.3 million per nerve. They confirmed the high density of small fibers in the area of the optic nerve known to carry macular fibers and noted loss of these small-caliber fibers following foveal photocoagulation in the monkey. Therefore, both anatomically and functionally the optic nerves and chiasm may be considered macular projection structures (Fig 4-9). The larger caliber, peripheral retinal axons subserving extramacular visual space tend to be distributed toward the periphery of the optic nerve, but intermingling of fibers without strict boundaries is the rule. Fibers that originate in the inferior retina remain inferior in the nerve and chiasm. The probable retinotopic organization of visual fibers in the optic nerves, chiasm, and tracts is demonstrated in Figure 4-10.

The arrangement of visual axons becomes considerably more complex in the lateral geniculate body, where a pattern of cellular layers is seen (Fig 4-7). The extent of macular representation in humans has been well documented by Kupfer (22). Focal vascular lesions of the geniculate bodies are only rarely recognized; this may be attributed to a dual blood supply via the anterior choroidal branch of the middle cerebral artery and the thalamogeniculate branches of the posterior cerebral and lateral choroidal arteries.

As the geniculocalcarine radiations begin, the inferior retinal fiber projection (superior field) takes an indirect and variable course for a short distance anteriorly around the tip of the temporal horn of the lateral ventricle, forming Meyer's loop.

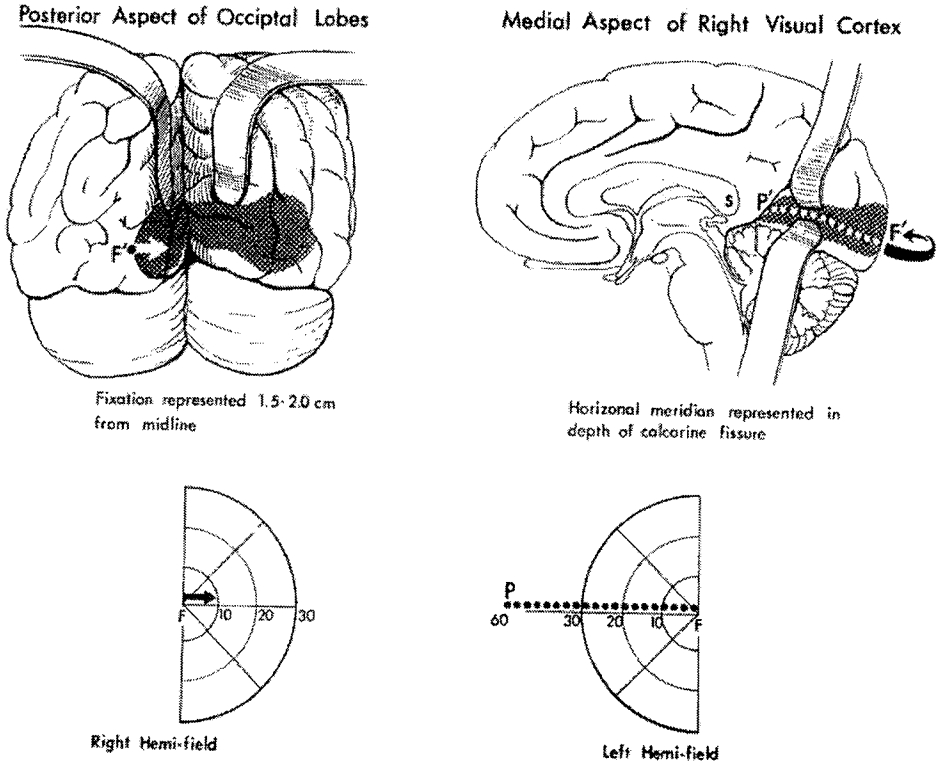


Fig 4-8. Location of visual cortex primarily in interhemispheral fissure. Lateral extension as illustrated is variable. Point F′ corresponds to central fixation point F in contralateral field. Peripheral field point P is represented in rostral portion of cortex, P′. S, splenium of corpus callosum.

In the parietal midradiations, superior peripheral fibers are seemingly separated from inferior peripheral fibers by the mass of macular-projection fibers. Further details of the distribution of fibers in the visual radiations may be found in the works of Spalding (23) and Van Buren and Baldwin (24).

The currently accepted conceptualization of the projection of the visual field on the occipital cortex is attributable primarily to the British neurologist Holmes (25), who studied visual field defects following head injuries in World War I. Spalding also took advantage of material that accrued during World War II by examining visual field defects following high-velocity, penetrating head injuries (26). The representation of the visual field in the occipital cortex as modified from the work of Holmes and Spalding is outlined in Figure 4-11.

The topographic anatomy of the human primary visual cortex has been studied (27) with regard to the area, distribution, and variability of the striate cortex on the surface and within the fissures of the occipital lobe. The following conclusions may be drawn: only approximately one third of the striate cortex is on the surface of the occipital lobe, the major portion lying buried in the calcarine fissure, its branches, and accessory sulci; as a rule, only a small portion (average 3% of total area) of striate cortex is exposed on the posterolateral aspect of the occipital pole; the area of striate cortex below the calcarine fissure is greater than that located above (approximately 3:2), and the inferior gyrus extends 1 to 2 cm more anteriorly; the horizontal extent of the visual cortex is variable but usually measures approximately 5 cm from pole to anterior extreme (lower calcarine lip); there is variation in both area and general configuration when paired visual cortices from the same brain are compared.

Because of the aforementioned anatomic variations in visual cortices, no finite point-to-point retinotopic representation can be applied to the occipi-

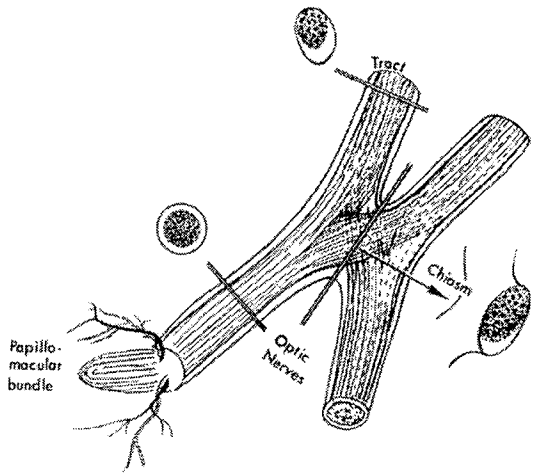


Fig 4-9. Representation of the macular (central field) projection in the anterior visual pathways. The majority of afferent visual fibers are related to the papillomacular bundle, which subserves the central visual field and comprises the central core of the optic nerve. Note that the crossing macular projection occupies an extensive area of the median bar of the chiasm.

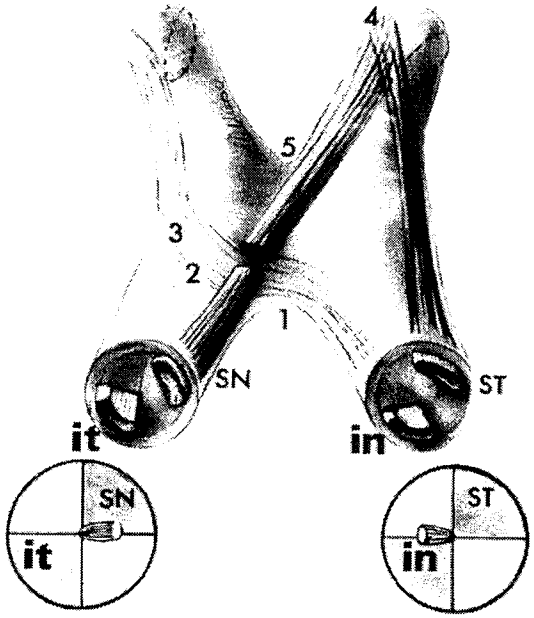


Fig 4-10. Retinotopic organization of visual fibers in the anterior visual pathways (after Hoyt). Diagram of homonymous retinal quadrants and their fiber projections, anterior aspect. it, inferior temporal; in, inferior nasal; SN, superior nasal; ST, superior temporal. Note the following: the superior fibers retain a superior course, and the inferior fibers retain an inferior position; the anterior notch (1) is occupied by inferonasal (superior temporal field) fibers; the inferonasal fibers bend slightly into the contralateral nerve (2), the von Wilband knee; inferior homonymous fibers converge in the chiasm (3) but superior homonymous fibers converge beyond the chiasm in the tract (4); the posterior notch (5) is occupied by superior nasal (inferior temporal field) fibers, as well as macular fibers (cf Fig 4-9).

tal lobe. Brindley (28) has reported the effects of electrode stimulation in the human visual cortex (as an attempt at visual prosthesis) in terms of evoked phosphenes in the visual field. Results are generally consistent with the established visual map of Holmes-Spalding, and no major amendments are required.

Regarding the retinotopic organization of the visual cortex, the following points deserve emphasis: (1) the macular field (including the foveal fixational area) is represented strictly unilaterally; (2) the central portion of field is represented in the caudal cortex, but the correspondence of field position (eg, 10°) with cortex locus (eg, 1 cm anterior to occipital pole) is uncertain; (3) the horizontal meridian of the visual field is represented in the depth of the calcarine fissure; (4) the vertical meridian of the visual field is represented in the periphery of the striate cortex; and (5) the unpaired monocular temporal crescent is represented in the most anterior aspect of the calcarine cortex.

VASCULAR SUPPLY

The vascular supply of the optic disc is derived principally from the incomplete arterial anastomotic circle of Zinn-Haller (Fig 4-4), which receives contributions from the posterior ciliary arteries, pial arterial plexus, and the peripapillary choroid. The latter also sends small arterioles directly to the prelaminar disc substance. The central retinal artery nourishes the retina but probably contributes very little to the nerve itself.

The intraorbital portion of the optic nerve is vascularized by perforating arteries derived from branches of the ophthalmic artery. In the optic canal and suprasellar space the nerve receives small pial branches of the internal carotid, anterior cerebral, and anterior communicating arteries.

The arterial supply of the chiasm may be divided into a superior and inferior group of vessels (17). The superior group is comprised of multiple small branches from the precommunicating portions of

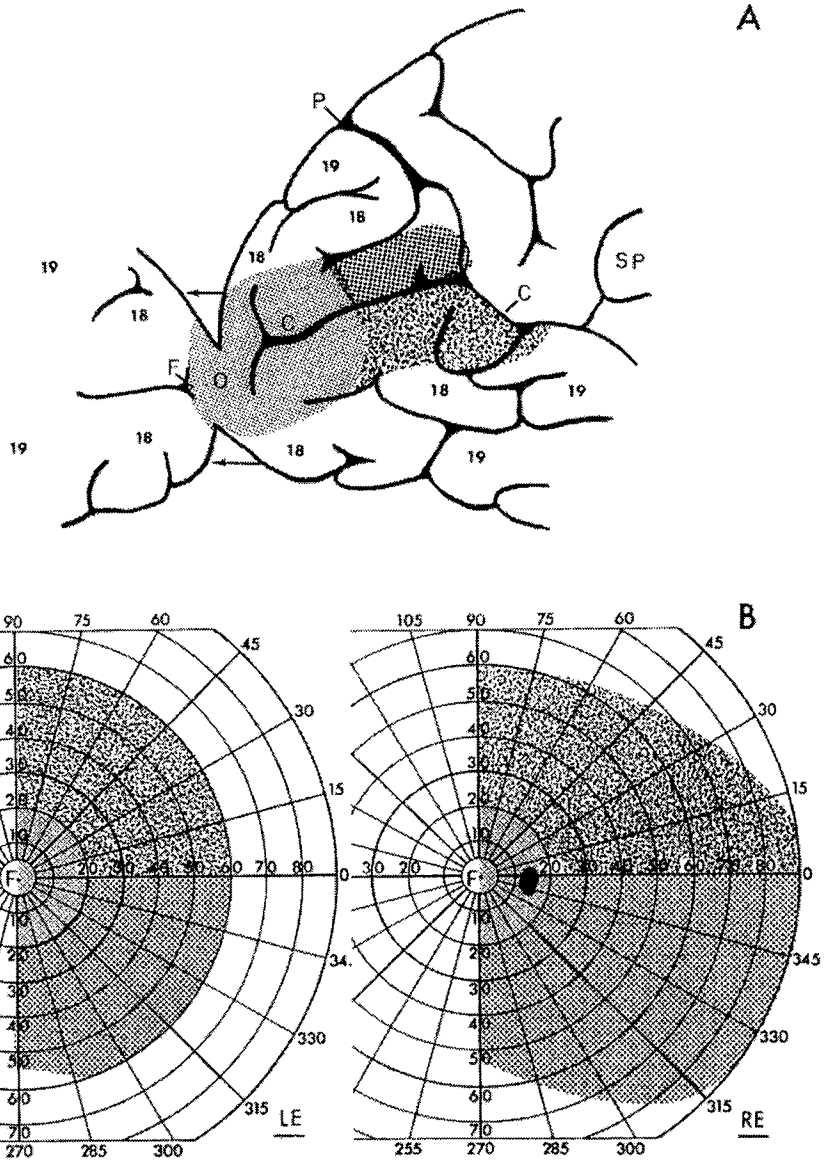


Fig 4-11. Occipital lobe and the corresponding projection of the visual field. **A.** Mesial aspect of left occipital lobe. The posterior pole (O) is flattened to illustrate the lateral surface (*arrows*) which is composed primarily of areas 18 and 19. The extension of striate cortex onto the lateral surface of the occipital pole is variable. The calcarine fissure (C) separates the striate or calcarine cortex into an upper and a larger lower strip, which also extends further forward toward the splenium (SP) of the corpus callosum. The visual cortex is approximately 5 cm in horizontal diameter, and the macular projection (*fine stipple*) may occupy as much as the posterior 2.5 cm. The border zone between macular and peripheral retinal cortical projections is arbitrarily illustrated. **B.** The right hemifields. Note that the upper field is represented in the inferior calcarine strip and the lower field in the superior calcarine strip. The central field has a disproportionately large cortical representation. F, point of fixation. The temporal field of the right eye extends to 90° as compared to the nasal 60° limit of the left eye. This 30° monocular temporal crescent is represented only in the contralateral hemisphere at the rostral extreme of the striate cortex.

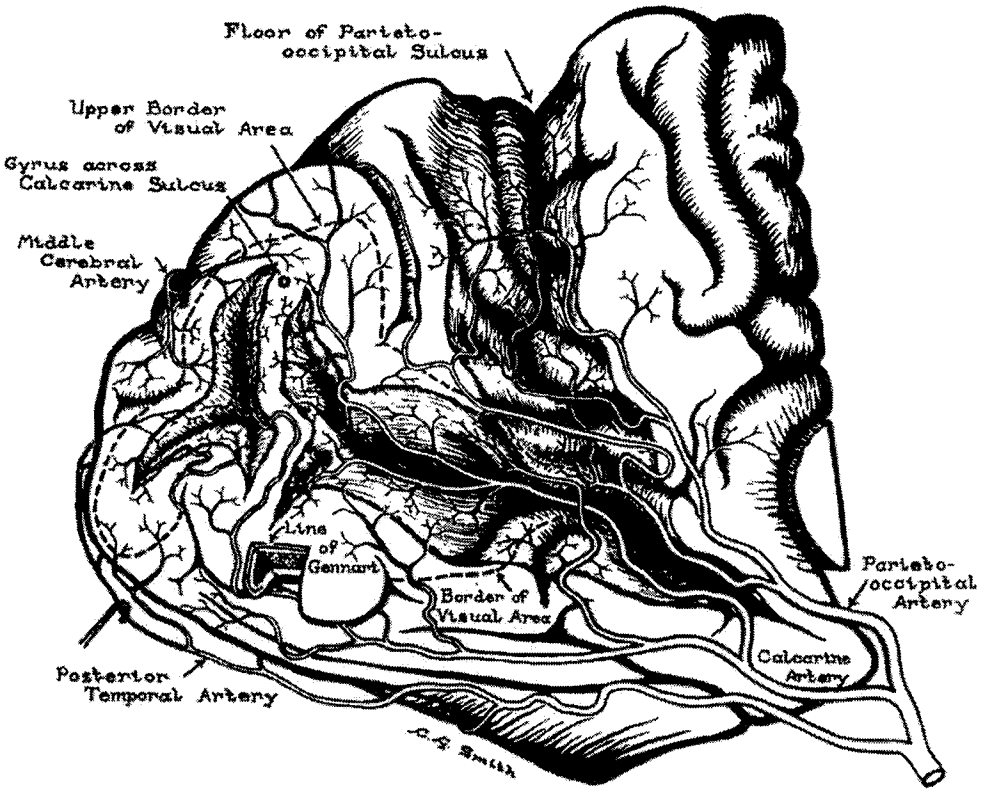
the anterior cerebral arteries. These vessels supply the upper surface of the optic nerves and tracts and the lateral portions of the chiasm. The inferior group of vessels is an extremely rich, anastomotic system designated as the superior hypophyseal arteries, derived from the internal carotids and posterior communicating and posterior cerebral arteries.

Anterior thalamic perforating branches of the posterior cerebral artery supply the optic tract, while thalamogeniculate branches supply the lateral geniculate body. A branch of the middle cerebral artery, the anterior choroidal artery, also supplies the tract and lateral geniculate body.

The initial portions of the visual radiations may receive a branch of the middle cerebral artery, the deep optic artery, which passes through the putamen to the internal capsule. Branches of the middle cerebral artery in the sylvian fissure (eg, the inferior temporo-occipital artery) variably supply the temporal radiations. The superior temporo-occipital sylvian artery is the major blood supply of the posterior radiations and can anastomose with posterior cerebral vessels at the occipital pole, providing a dual blood supply to the visual cortical convexity. This arterial configuration has been used to explain "macular sparing" which characterizes some cortical hemianopsias.

The posterior cerebral artery (PCA) courses around the midbrain between the cerebral peduncle and the hippocampal gyrus of the temporal lobe, the inferior aspect of which is supplied by the anterior temporal artery, the first cortical branch of the PCA. The remaining three major cortical branches of the PCA may all contribute to the visual cortex: the posterior temporal, calcarine, and parieto-occipital arteries (Fig 4-12). The blood supply of the striate cortex is usually primarily by the calcarine artery, but branches of the other two afore-

Fig 4-12. Blood supply of striate cortex. Medial surface of left occipital lobe with visual cortex outlined by broken line. Calcarine and parieto-occipital fissures are opened to show course of cortical branches of posterior cerebral artery. Note potential triple supply to macular area, via the calcarine, posterior temporal, and middle cerebral arteries. (From Smith CG, Richardson WFG.: The course and distribution of the arteries supplying the visual (striate) cortex. Am J Ophthalmol 61:1391, 1966.)



mentioned vessels commonly share this responsibility and may account for preserved portions of field, including the macular area, despite calcarine artery occlusion (29). The terminal branches of the middle cerebral artery also supply the posterior aspect of the occipital pole.

EXTRAGENICULOSTRIATE VISUAL SYSTEMS

It is increasingly evident that nonstriate visual systems exist in animals and almost surely in man. Retinotopic organization of the visual field in the superior colliculus has been established in the monkey (30), relating that structure to visually guided behavior and eye movement. Cells of the monkey colliculus respond to moving stimuli within specific receptor fields, and stimulation of these collicular cells results in reciprocal saccadic eye movement toward the specific visual field area.

The interrelationship between the visual cortex and the superior colliculus is not yet clarified, but the visual acquisition of a target with accurate saccadic eye movements may be dependent on collicular function. In essence it would appear that the tectum has distinctive functions in movement detection, stimulus location, and integration of eye movements with auditory, tactile, and visual stimuli.

Although subjective visual phenomena have been recorded during subcortical (optic radiations and posterior hippocampus) (31) and brainstem (32) stimulation in man, as yet clinical application is uncertain. In patients cortically blind for all other visual stimuli, the recognition of sudden changes in illumination has been documented (33).

REFERENCES

1. Bruesch SR, Arey LB: The number of myelinated and unmyelinated fibers in the optic nerve of vertebrates. J Comp Neurol 77:631, 1942
2. Dowling JE: Organization of vertebrate retinas. Invest Ophthalmol 9:655, 1970
3. Werblin FS: The control of sensitivity in the retina. Sci Am 228:70, 1973
4. Østerberg G: Topography of the layer of rods and cones in the human retina. Acta Ophthalmol suppl 6, 1935
5. Van Buren JM: The Retinal Ganglion Cell Layer. Springfield, IL: Thomas, 1963, p 130
6. Glaser JS: The nasal visual field. Arch Ophthalmol 77:358, 1967
7. Ogden TE: The nerve-fiber layer of the primate retina: An autoradiographic study. Invest Ophthalmol 13:95, 1974
8. Anderson DR, Hoyt WF: Ultrastructure of intraorbital portion of human and monkey optic nerve. Arch Ophthalmol 82:506, 1969
9. Anderson DR: Ultrastructure of meningeal sheaths: Normal human and monkey optic nerves. Arch Ophthalmol 82:659, 1969
10. Anderson DR: Ultrastructure of human and monkey lamina cribrosa and optic nerve head. Arch Ophthalmol 82:800, 1969
11. Anderson DR: Ultrastructure of the optic nerve head. Arch Ophthalmol 83:63, 1970
12. Anderson DR: Vascular supply of the optic nerve of primates. Am J Ophthalmol 70:341, 1970
13. Hayreh SS: Anatomy and physiology of the optic nerve head. Trans Am Acad Ophthalmol Otolaryngol 78:240, 1974
14. Tenner MS, Trokel SL: Demonstration of the intraorbital portion of optic nerves by pneumoencephalography. Arch Ophthalmol 79:572, 1968
15. Walker AE: The neurosurgical evaluation of the chiasmal syndromes. Am J Ophthalmol 54:563, 1962
16. Bergland RM, Ray BS, Torack RM: Anatomical variations in the pituitary gland and adjacent structures in 225 human autopsy cases. J Neurosurg 28:93, 1968
17. Bergland RM, Ray BS: The arterial supply of the human optic chiasm. J Neurosurg 31:327, 1969
18. Hoyt WF, Luis O: Visual fiber anatomy in the infrageniculate pathway of the primate: Uncrossed and crossed retinal quadrant fiber projections studied with Nauta silver stain. Arch Ophthalmol 68:94, 1962
19. Hoyt WF, Luis O: The primate chiasm: Details of visual fiber organization studied by silver impregnation techniques. Arch Ophthalmol 70:69, 1963
20. Hoyt WF, Tudor RC: The course of parapapillary temporal retinal axons through the anterior optic nerve: A Nauta degeneration study in the primate. Arch Ophthalmol 69:503, 1963
21. Potts AM, Hodges D, Shelman CB, et al: Morphology of the primate optic nerve: I–III. Invest Ophthalmol 11:980, 1972
22. Kupfer C: The projection of the macula in the lateral geniculate nucleus of man. Am J Ophthalmol 54:597, 1962
23. Spalding JMK: Wounds of the visual pathway: I. The visual radiation. J Neurol Neurosurg Psychiatry 15:99, 1952
24. Van Buren JM, Baldwin M: The architecture of the optic radiation in the temporal lobe of man. Brain 81:15, 1958
25. Holmes G: A contribution to the cortical representation of vision. Brain 54:470, 1931
26. Spalding JMK: Wounds of the visual pathway: II. The striate cortex. J Neurol Neurosurg Psychiatry 15:169, 1952
27. Stensaas MA, Eddington DK, Dobelle WH: The topography and variability of the primary visual cortex in man. J Neurosurg 40:747, 1974

28. Brindley GS: Sensory effects of electrical stimulation of the visual and paravisual cortex in man. In Jung R (ed): Handbook of Sensory Physiology. Berlin: Springer-Verlag, 1973, vol VII/3B, pp 583–594
29. Smith CG, Richardson WFG: The course and distribution of the arteries supplying the visual (striate) cortex. Am J Ophthalmol 61:1391, 1966
30. Schiller PH: The role of the monkey superior colliculus in eye movement and vision. Invest Ophthalmol 11:451, 1972
31. Adams JE, Rutkin BB: Visual responses to subcortical stimulation in the visual and limbic systems. Confina Neurol 32:158, 1970
32. Nashold BS: Phosphenes resulting from stimulation of the midbrain in man. Arch Ophthalmol 84:433, 1970
33. Brindley GS, Gautier-Smith PC, Lewin W: Cortical blindness and the functions of the non-geniculate fibres of the optic tracts. Neurol Neurosurg Psychiatry 32:259, 1969

15

The Pupils and Accommodation

THOMAS L. SLAMOVITS
JOEL S. GLASER

The pupil is a kinetic indicator of both ocular motor function and the special sensory apparatus, the retina, which it serves. The neural mechanisms that control pupil size and reactivity are highly complex, yet they may be sampled and evaluated by simple clinical procedures. Pupillary function depends on the integrity of the structures along the course of the pupillomotor pathway (Fig. 1): (1) retinal receptors, (2) ganglion cell axons in the optic nerve, (3) chiasm and (4) optic tract (but not the lateral geniculate body), (5) brachium of the superior colliculus, (6) pretectal area of the mesencephalon, (7) the interconnecting neurons to pupilloconstrictor motor cells in the oculomotor nuclear complex, (8) the efferent parasympathetic outflow accompanying the third cranial nerve, and (9) the efferent sympathetic pathway from the hypothalamus to the pupillary dilator muscle. In addition, the size of the pupils is influenced by the intensity of retinal illumination, the near-effort reflex, the state of retinal light adaptation, by supranuclear influences from the frontal and occipital cortex above the pretectal area and from the reticular formation of the brain stem below.

At a given moment, any or all of the above factors may influence pupillary size and reactivity. It should be no wonder, then, that in the awake state the pupil is rather constantly moving, a condition of physiologic unrest termed *hippus*. This incessant change in pupil size has no pathologic significance;[1] although it is described in diverse conditions ranging from encephalitis to schizophrenia and from cataracts to hemorrhoids. Age affects both pupillary size and reactivity.[2,3] The pupil of the neonate is miotic but increases in size during the first decade of life; from the second decade on, the pupil steadily becomes smaller (Fig. 2). Pupillary reactivity, at least to "long" (3-second) light flashes, also seems related to age; the range of amplitude of the light reflex declines with increasing age (Fig. 3).

The pupil may be considered to have three major optic functions: (1) to regulate the amount of light reaching the retina; (2) to diminish the chromatic and spherical aberrations produced by the peripheral imperfections of the optical system of the cornea and lens; and (3) to increase depth of field (analogous to the f-stop setting of a camera).

As pupillary size increases, so does chromatic and spherical aberration. As pupillary size decreases, light diffraction at the pupil edge becomes a more significant factor in reducing image quality; this generally outweighs any benefit of miosis-induced increase in focal depth. In their experiments of optical line-spread function, Campbell and Gubisch[4] found the optimal pupil diameter to be 2.4 mm; scatter and focusing defects have an increasing effect with larger pupils.

ANATOMICAL CONSIDERATIONS

Mechanically, the diameter of the pupil is determined by the antagonistic actions of the iris sphincter and dilator muscles, with the radially arranged dilator fibers playing the minor role. The sphincter, which can be seen in light or atrophic irides, is attached to contiguous iris tissues along its circumference. Rather than retracting toward one quadrant when severed or ruptured, the sphincter continues to function except in the altered segment. Therefore, with prudence, the pupillary reactions may be evaluated even in the presence of iris atrophy, traumatic rupture of the sphincter, or surgical colobomas.

LIGHT REFLEX PATHWAY

The pupillary light reflex pathway may functionally be considered a three-neuron arc (see Fig. 1): the afferent neurons from retinal ganglion cells to the pretectal area; an intercalated neuron from the pretectal complex to the parasympathetic motor pool (Edinger-Westphal nucleus) of the oculomotor nuclear complex; and the parasympathetic outflow with the oculomotor nerve to the ciliary ganglion, and from there to the pupillary sphincter.

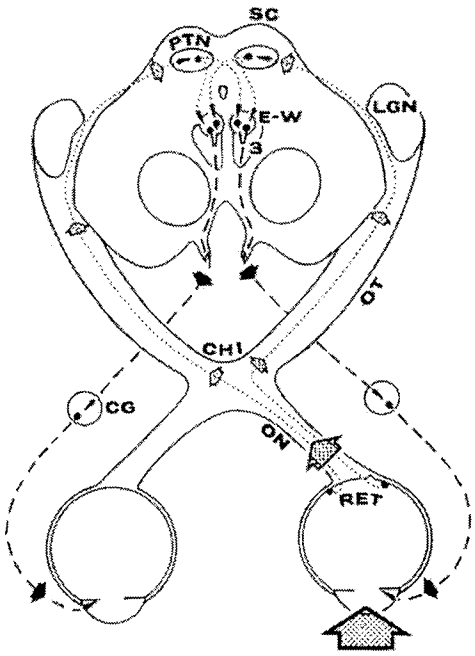


Fig 1. Pupillary light reflex. Light in left eye (*dotted arrow*) stimulates retina (*RET*), whose afferent axons (*fine dashed lines*) ascend optic nerve (*ON*), decussate at chiasm (*CHI*), and terminate in pretectal nuclear complex (*PTN*). Lateral geniculate nucleus (*LGN*) is bypassed by these pupillomotor fibers. The PTN is connected by crossed and uncrossed intercalated neurons to both Edinger-Westphal parasympathetic motor nuclei (*E-W*), which comprise the dorsal aspect of the oculomotor nuclear complex (*3*). Preganglionic parasympathetic fibers (*heavy dashed lines*) leave ventral aspect of midbrain in the substance of the third cranial nerves. After synapsing in the ciliary ganglia (*CG*), the postganglionic fibers innervate the pupillary sphincter muscles. Note that uniocular light stimulus evokes bilateral and symmetric pupillary constriction. Brain stem diagram represents section through level rostral to superior colliculi (*SC*).

Considerable evidence exists that the visual cells of the retina, (i.e., the rods and cones) also serve as light receptors controlling pupillomotor activity. For example, pupillomotor light thresholds follow the same shifts in spectral sensitivity as visual thresholds, depending on the state of light adaptation of the retina (Purkinje shift). Pupillomotor sensitivity of the retina also parallels visual form sensitivity, which is highest at the fovea and lowest in the periphery. In our present state of knowledge, it seems that the same afferent axons in the optic nerve transmit pupillomotor information to the pretectal area and visual information to the lateral geniculate nuclei. That this dual function is accomplished by axonal bifurcation in the optic tract is suspected but unproved in humans.[5] Therefore, we may consider two intimately related systems: retinogeniculate for visual perception, and retinomesencephalic for pupillomotor control.

At the optic chiasm, slightly more than one half of the afferent axons in the optic nerve cross to the opposite optic tract, where they are mixed with noncrossing axons from the contralateral optic nerve. The ratio of crossed to uncrossed fibers is about 53:47.[6] From the chiasmal level posteriorly, afferent visual and pupillomotor information from either eye is divided into crossed fibers (from nasal retinal receptors of the contralateral eye) and uncrossed fibers (from temporal retinal receptors of the ipsilateral eye). In the posterior aspect of the optic tract (pregeniculate), the pupillomotor branches of the afferent axons gain the pretectal nuclear area by transversing the brachium of the superior colliculus into the rostral midbrain. Intercalated neurons interconnect to the Edinger-Westphal nuclei by crossing dorsal to the aqueduct in the posterior commissure and by coursing ventrally in the periaqueductal gray matter. This simplistic anatomical approach belies the true complexity of the neurophysiology and neuroanatomy of the pretectal nuclear complex. The reader is referred to articles by Smith and co-workers[7] Carpenter and Pierson,[8] Benevento and associates[9] and Burde.[10]

The organization of the oculomotor nuclear complex in the rostral mesencephalon (midbrain) is considered as depicted by Warwick in 1953[11] and Jampel and Mindel in 1967.[12] The anteromedian nucleus (Edinger-Westphal) is the source of special visceral efferent motor axons to the iris sphincter and ciliary musculature. This dorsal cell mass may be subdivided into a rostral portion associated with accommodation, a caudal portion the stimulation of which produces pupil constriction, and a midportion associated with both accommodation and constriction. According to the degeneration studies by Warwick, the ciliary ganglion contains more cells for innervation of the ciliary muscles than for innervation of the iris sphincter (approximately 30:1). Presumably, that same ratio occurs in the Edinger-Westphal nucleus.

From the parasympathetic nucleus, the pupillomotor and ciliary fibers join the outflow of the oculomotor nuclei and exit from the substance of the midbrain with the oculomotor nerves in the interpeduncular space. According to Kerr and Hollowell,[13] the pupillomotor fibers are superficially located in the nerve, lying just internal to the epineurium. It is thought that this superficial posi-

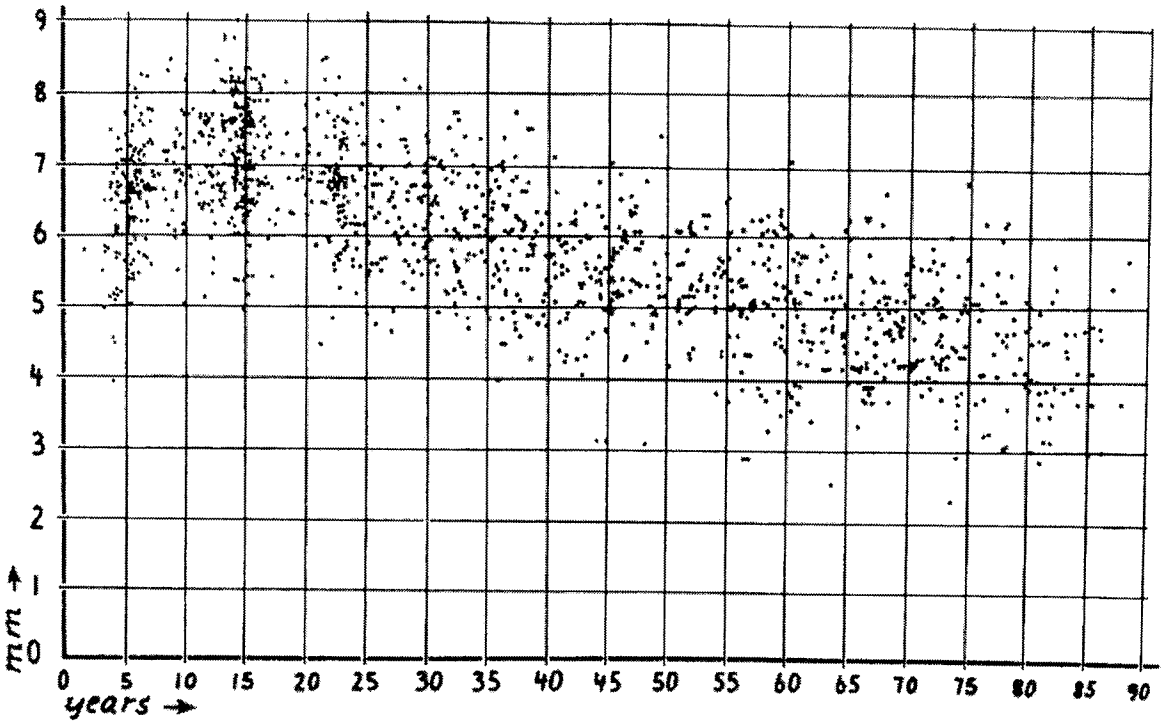


Fig 2. Pupillary size in darkness of 1263 subjects chosen at random; average pupil size was used [(R + L)/2]. Abscissa shows horizontal diameters in millimeters, ordinate shows subjects' age in years. Note the wide scatter but obvious age trend. See also Figure 3, top curve. (Reprinted with permission from Loewenfeld IE: Pupillary changes related to age. In Thompson HS, Daroff RB, Frisen L et al (eds): Topics in Neuro-ophthalmology, p 129. Baltimore, Williams & Wilkins, 1979)

tion makes the pupillomotor fibers especially vulnerable to compression. However, in more anterior segments (*e.g.*, the cavernous sinus), pupillomotor fibers may be preferentially spared even in the presence of total oculomotor palsy. It is likely that involvement or "sparing" of the pupil sphincter reflects the nature and acuteness of the injury rather than merely the portion of the third nerve that is compromised.[14]

At approximately the level of the superior orbital fissure, the oculomotor nerve divides into superior and inferior divisions, with parasympathetic fibers traveling in the latter to the ciliary ganglion via the branch to the inferior oblique muscle. Although the ciliary ganglion contains afferent sensory fibers (nasociliary nerve) and sympathetic fibers to the vessels of the globe and dilator of the iris, only the parasympathetic fibers synapse here. The parasympathetic postganglionic fibers then pass to the globe via the short ciliary nerves.

The weight of anatomical evidence supports the view that the parasympathetic pupillomotor fibers synapse in the ciliary ganglion.[15] However, some experimental studies in monkeys, using horseradish peroxidase (HRP) techniques, suggest the presence of a nonsynapsing pathway between the midbrain and the eye.[16,17] The latter view may be supported clinically by cases of preciliary ganglionic anisocoria with hypersensitivity to low-concentration parasympathetic agents.[18,19]

The pretectal pupilloregulator mechanism is subject to a variety of supranuclear influences, which may be summarized as follows: (1) *excitatory*, retinomesencephalic (light stimulus) and occipitomesencephalic (near reflex); and (2) *inhibitory*, corticomesencephalic and hypothalamomesencephalic pathways and the ascending reticulomesencephalic system. During sleep and obtunded states, these supranuclear inhibitory influences are diminished, with resultant miotic but reactive pupils. Arousal results in mydriasis due to

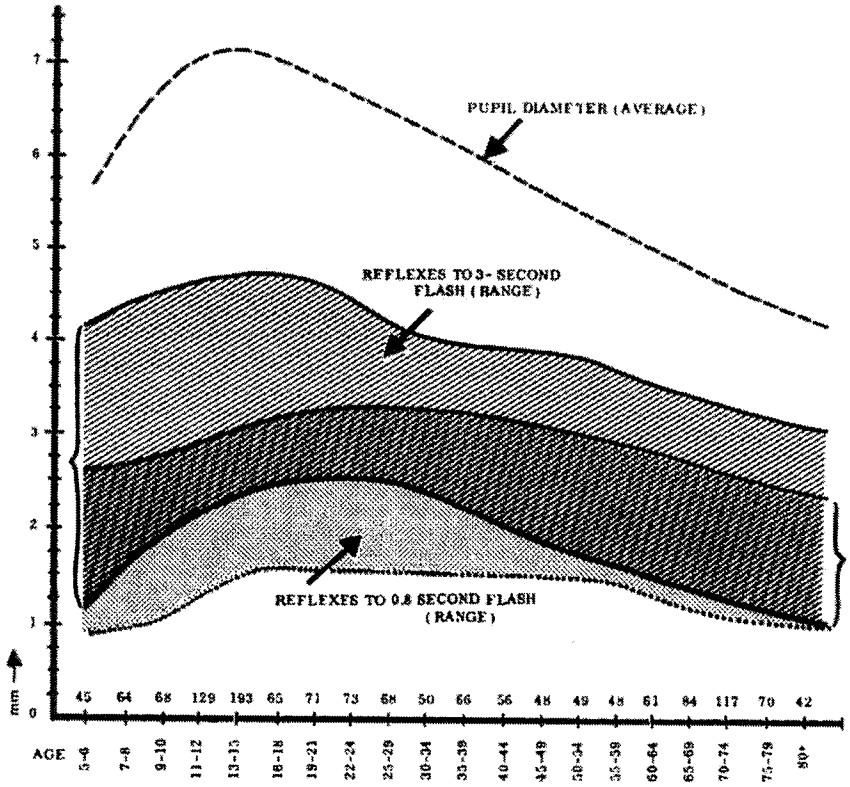


Fig 3. Normal ranges of light reflex amplitude for long and for short flashes. Shaded area (*left bracket*) is normal range for 3-second flashes; stippled area is normal range for 0.8-second flashes. The numbers above the abscissa indicate the number of subjects per age-group. Note early peak, followed by decline with age for reactions to long light flashes. In contrast, reflexes elicited by short flashes show relatively flat age curve. (Reprinted with permission from Loewenfeld IE: Pupillary changes related to age. In Thompson HS, Daroff RB, Frisen L et al (eds): Topics in Neuro-ophthalmology, p 137. Baltimore, Williams & Wilkins, 1979)

the return of supranuclear inhibition, and sympathectomy does not eliminate this dilatation.

OCULAR SYMPATHETIC PATHWAYS

Sympathetic outflow to the iris dilator muscles begins in the posterolateral area of the hypothalamus and descends uncrossed through the tegmentum of the midbrain and pons (Fig. 4). At the level of the medulla the sympathetics lie laterally, where they may be affected in lateral medullary plate infarction (*i.e.*, Wallenberg's syndrome). The descending fibers, considered first-order preganglionic neurons, terminate in the intermediolateral cell column at the C8 to T2 cord level (the ciliospinal center of Budge). Second-order preganglionic fibers exit the cord primarily with the first ventral thoracic root (T1), but some pupillomotor sympathetics egress with C8 or T2. Via the white rami communicantes, the fibers enter the paravertebral sympathetic chain, which is closely related to the pleura of the lung apex. At this location the sympathetics may be affected by neoplasms, (*i.e.*, the Pancoast's syndrome; see discussion of Horner's syndrome).

The fibers detour with the ansa subclavia around the subclavian arteries, ascend without synapsing through the inferior and middle cervical ganglia, and terminate in the superior cervical ganglion at the base of the skull. Third-order postganglionic oculosympathetic fibers ascend the internal carotid to enter the skull, whereas fibers for sweat and piloerection of the face follow the external carotid and its branches.

The intracranial sympathetics to the eye follow a circuitous course: (1) fibers to the tympanic plexus of the middle ear and petrous bone; (2) fibers temporarily joining the path of the intracavernous abducens nerve before anastomosing with the first division of the trigeminal nerve; (3) anastomoses with the ophthalmic–trigeminal (the primary pupillomotor pathway via the nasociliary nerve); and (4) fibers to the ophthalmic artery and ocular motor nerves at the level of the cavernous sinus. Postganglionic sympathetics include (1) orbital vasomotor fibers, (2) pupillary dilators, (3) smooth muscles of the upper and lower lids (Müller), (4) lacrimal gland, and (5) trophic fibers to uveal melanophores. Vasomotor

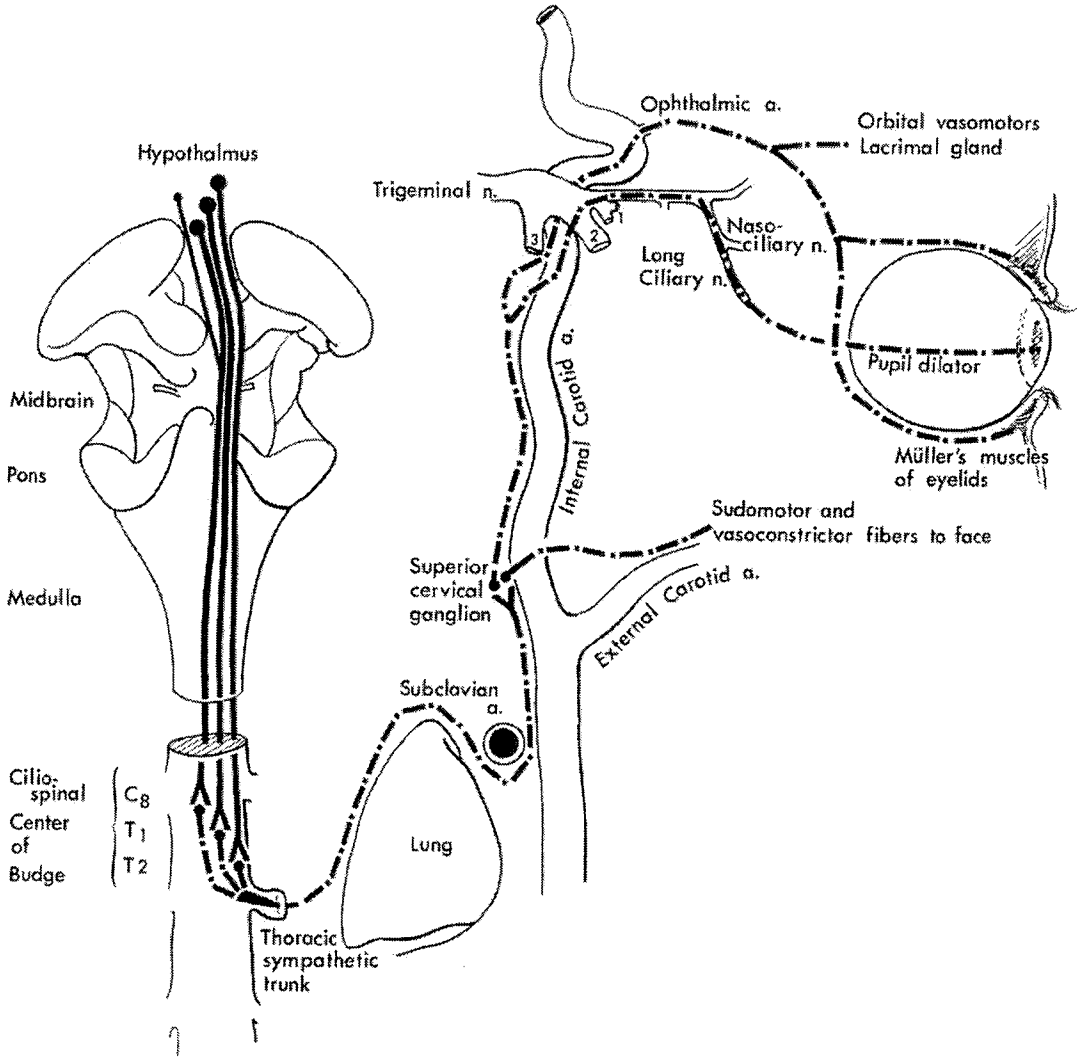


Fig 4. Ocular sympathetic pathways. Hypothalamic sympathetic fibers comprise a polysynaptic (?) system as they descend to the ciliospinal center. This intra-axial tract is functionally considered the "first-order neuron." The second-order neuron takes a circuitous course through the posterosuperior aspect of the chest and ascends in the neck in relationship to the carotid system. Third-order neurons originate in the superior cervical ganglion and are distributed to the face with branches of the external carotid artery and to the orbit via the ophthalmic artery and ophthalmic division (*1*) of the trigeminal nerve.

sympathetics to the globe pass without synapse through the ciliary ganglion and short posterior ciliary nerves.

NEAR REFLEX AND ACCOMMODATION

With accommodative effort, caused either by a blurred retinal image or conscious visual fixation on a near object of regard, a "near synkinesis" is evoked, including (1) increased accommodation of the lens, (2) convergence of the visual axes of the eyes, and (3) pupillary constriction. The neural mechanisms of this motor triad are in no way as well understood as the pathways for pupillary light reactions or the saccadic and pursuit ocular motor systems. It is likely that awareness of decreased

object distance evokes accommodative effort originating in frontal centers; blurred retinal images are sensed in the occipital cortex and corrected via occipitotectal tracts. Jampel[20] obtained increased bilateral accommodation, convergence, and usually miosis by unilateral stimulation of the peristriate cortex (area 19) in primates. A midbrain "center" for accommodative vergence is suggested on theoretical grounds[21] but has not yet been anatomically verified. However, the anteromedian nucleus (Edinger–Westphal) of the oculomotor complex in the rostral midbrain has been mapped stereotactically[12] and may be divided functionally into a rostral portion concerned with accommodation, a caudal portion that elicits pupillary constriction, and a middle segment that, when stimulated, results in accommodation and constriction.

The final pathway for pupil constriction, whether evoked by light or accommodative effort, consists of the oculomotor nerve, ciliary ganglion, and short posterior ciliary nerves. The ratio of ciliary ganglion cells innervating ciliary muscle to cells innervating the iris sphincter is approximately 30:1.

Pupillary constriction evoked by the near reflex is not as easily evaluated as the light reaction. Accommodative vergence is under voluntary control, and the success of this maneuver is very much dependent on the patient's cooperation and capacity to converge. In the elderly, convergence is diminished and the near reflex is especially difficult to test. An accommodative target is helpful, including the use of the patient's own fingertips. Vision itself is not a requisite for the near response, which can be tested in the blind by proprioceptive "fixation" of the patient's fingertips. Indeed, accommodation and convergence may be held in abeyance by substituting plus lenses and base-out prisms, without eliminating pupillary constriction.

If pupillary reactions are brisk to light stimulus, the near reactions need not be examined. However, it is important for the student to learn this examination technique and to become acquainted with the limits of normality. The light and near efforts are additive, that is even with the eye brightly illuminated, further pupillary constriction is observed when gaze is shifted from distance to near. Therefore, when testing the light reflex, gaze (accommodation) should be steadily controlled by fixation on a distant target. If the pupil fails to react to light, the eye may be fully illuminated while examining the near reflex.

THE PATIENT WITH ABNORMAL PUPILS

In office practice, patients present with relatively few isolated "pupil" problems, including the tonic pupil syndrome, pharmacologic accidents, sympathetic paresis (Horner's syndrome), pupillary light–near dissociation, Argyll Robertson pupils, and essential anisocoria (Table 1). It is extremely unlikely that a patient with a posterior communicating aneurysm or other basal tumor will present with only an abnormal pupil and no ocular motor or sensory disturbances. The reader is referred to the index to these volumes to locate a more detailed discussion of pupillary findings with posterior communicating artery aneurysms. Direct trauma to the anterior ocular segment, local disease of the iris (*e.g.*, cyst, melanoma, rubeosis, sphincter rupture, iritis), and angle-closure glaucoma are slit-lamp diagnoses that need not be discussed here, other than to point out that such local iris lesions have been misinterpreted as neurologic deficits.

RELATIVE AFFERENT PUPILLARY DEFECT

When there is a significant unilateral or asymmetric visual deficit caused by retinal or optic nerve disease, the pupils will show a subnormal response to light stimulation of the eye with the greater field or (generally) acuity loss. The pupils will have a more extensive constriction response with light stimulation of the normal or less involved eye. It is this combination of subnormal direct pupillary light response and a normal indirect (consensual) response when the opposite eye is illuminated that constitutes the relative afferent pupillary defect (RAPD) (Fig. 5). The RAPD can be clinically demonstrated by the alternate cover test, also termed *Gunn's pupillary test*, as described by Kestenbaum,[22] or by the swinging flashlight test of Levatin.[23]

The swinging flashlight test is best performed in a dimly lighted room, using a bright light (see below) such as a muscle light or penlight. During the test, the patient must look at a distant fixation target to avoid accommodative miosis.

The test light is shone directly into the visual axis to illuminate first one pupil and then the other. The alternating or *swinging* light should pause 3 to 5 seconds in each eye, and this maneuver should be repeated several times. As a rule, the pupils are round and practically equal in diameter (see below, Essential Anisocoria) and briskly and symmetrically reactive to light stimuli. After an initial, prompt pupil constriction, a slight "release" dila-

TABLE 1. Characteristics of Pupils Encountered in Neuro-ophthalmology

	General Characteristics	Responses to Light and Near Stimuli	Room Condition in which Anisocoria is Greater	Response to Mydriatics	Response to Miotics	Response to Pharmacologic Agents
Essential anisocoria	Round, regular	Both brisk	No change	Dilates	Constricts	Normal and rarely needed
Horner's syndrome	Small, round, unilateral	Both brisk	Darkness	Dilates	Constricts	Cocaine 4%, poor dilation Paredrine 1%, no dilation if third-order neuron damage
Tonic pupil syndrome (Holmes-Adie syndrome)	Usually larger* in bright light; sector pupil palsy, vermiform movement Unilateral or, less often, bilateral	Absent to light, tonic to near; tonic redilation	Light	Dilates	Constricts	Pilocarpine 0.1% or 0.125% constricts; Mecholyl 2.5% constricts
Argyll Robertson pupils	Small, irregular, bilateral	Poor to light, better to near	No change	Poor	Constricts	
Midbrain pupils	Mid-dilated; may be oval; bilateral	Poor to light, better to near (or fixed to both)	No change	Dilates	Constricts	
Pharmacologically dilated pupils	Very large†, round, unilateral	Fixed‡	Light		No‡	Pilocarpine 1% will not constrict
Oculomotor palsy (nonvascular)	Mid-dilated (6 mm–7 mm), unilateral (rarely bilateral)	Fixed	Light	Dilates	Constricts	

* Tonic pupil may appear smaller following prolonged near-effort or in dim illumination; affected pupil is initially large, but with passing time gradually becomes smaller.
† Atropinized pupils have diameters of 8mm to 9 mm. No tonic, midbrain, or oculomotor palsy pupil ever is this large.
‡ Pupils may be weakly reactive, depending on interim after instillation.

tion generally occurs. In the presence of, for example, a *right* afferent defect (see Fig. 5), the following will be observed with the swinging flashlight test: the pupillary diameters will be equal and slightly larger bilaterally when the right eye is stimulated and bilaterally smaller when the normal left eye is illuminated. If only the pupil being illuminated is observed, the other pupil being hidden in darkness, the following is seen: the normal left pupil will constrict promptly on illumination; as the light is rapidly moved to the right, the right pupil actually is seen to dilate or "escape"; as the light moves again to the left, the left pupil again constricts briskly.

Afferent pupillary defects may be conveniently quantitated by the use of neutral-density filters placed before the *normal* eye to "balance" or neutralize a positive (asymmetric) swinging light test.[24] Whether a dim, bright, or brilliant light is best suited for pupil light-reaction testing is somewhat controversial[25] but an indirect ophthalmoscope light set at 6 volts may be used as a handy "standardized" light source. Thompson and Jiang[26] stress the importance of avoiding asymmetric retinal bleach, by maintaining a rhythmic "equal time" alternation of the light from one eye to the other and by not swinging the light too many times between the eyes. Thompson and others[24,27] provide detailed guidelines for proper performance of the pupillary examination and assessment of the RAPD.

An afferent pupillary defect may be assessed even if one of the pupils is unreactive, whether due to mydriatics, miotics, oculomotor palsy, trauma

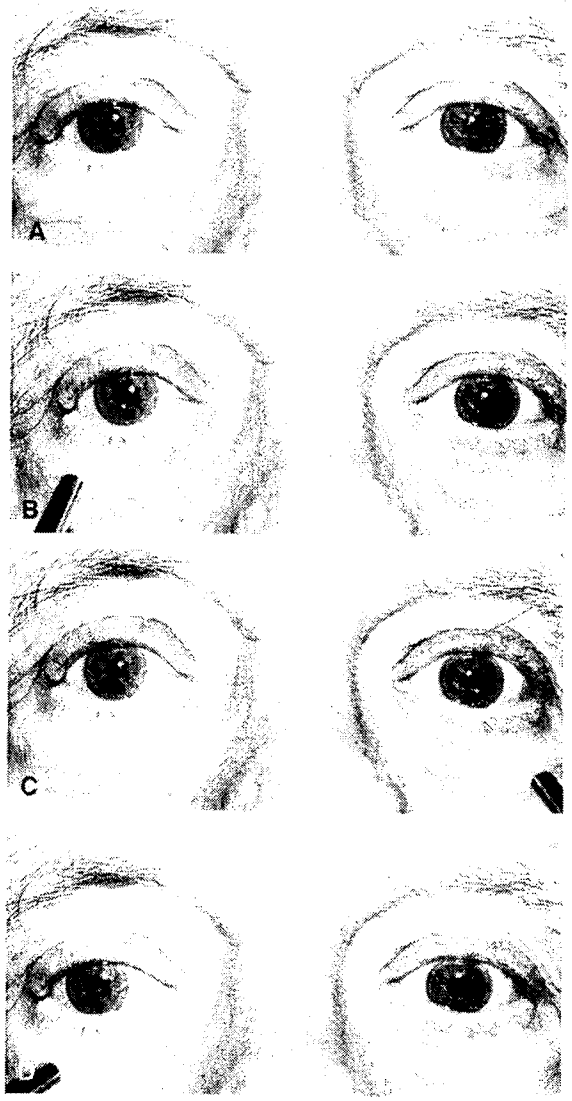


Fig 5. Swinging flashlight test for afferent pupil defect. The patient is a 72-year-old man with right visual loss due to ischemic optic neuropathy. (*A*) Pupils are equal in dim light. (*B*) Illumination of right eye results in modest bilateral constriction. (*C*) When the light swings to the left, there is more extensive constriction in both pupils. (*D*) When the light swings back to the right, both pupils dilate.

(Fig. 6) or synechial formation. In such cases, when performing the swinging flashlight test, the direct and consensual responses of the single reactive pupil must be compared. The reactive pupil's direct light response reflects the afferent function of the ipsilateral eye; its consensual response reflects the afferent function of the contralateral eye.

It should be emphasized that even severe unilateral visual loss due to retinal or optic nerve diseases associated with an afferent pupillary defect, is not of itself a cause of anisocoria, despite past statements to the contrary. If a patient with a RAPD also shows anisocoria, the pupillary inequality must be treated as a separate finding. The RAPD most typically provides objective evidence of optic nerve disease that is either unilateral or asymmetric, with more profound visual involvement on the side of the RAPD. In such cases the RAPD is not specific and may reflect optic neuropathy due to demyelination, ischemia, compression, or asymmetric glaucoma.

Because slightly more fibers cross than remain uncrossed at the level of the chiasm, RAPD's may also be seen with optic tract lesions, where greater visual field loss occurs in one eye. An obvious example would be an optic tract lesion with a complete homonymous hemianopia. In such a case, a relative afferent pupillary defect would be expected in the eye with the temporal visual field loss (*i.e.*, the eye contralateral to the side of the optic tract lesion).[28] Theoretically the same kind of RAPD could be present without any associated visual field defect if there is a contralateral lesion affecting the pupillomotor fibers between the optic tract and pretectal region. The eye with the RAPD should have normal visual acuity, color vision, and visual field, and no other (occult) cause for the pupillary defect (*i.e.*, no amblyopia, glaucoma, past optic neuritis). Ellis[29] has reported an afferent pupillary defect contralateral to a pineal region tumor, suggesting that this was due to involvement of afferent pupillary fibers between the optic tract and pretectal nucleus. Johnson and Bell have also documented a RAPD in a pretectal lesion due to a pineal gland mixed-cell tumor.[30]

RAPD can also be seen with diseases of the retina and macula. An extensive retinal detachment, for example, two quadrants detached, should cause an obvious RAPD, as will arterial occlusions. With unilateral or markedly asymmetric retinitis pigmentosa one should see a RAPD; however, usually the disease process is quite symmetric and thus a RAPD is typically not present.[31] The RAPD in general is proportional to the extent of visual field loss and, in fact, the size of the visual field defect is more closely correlated with the extent of the RAPD than is visual acuity loss.[32] As a rule, strictly macular disease leads to a much less profound afferent pupillary defect than the bulk of diseases affecting the optic